



BILLING CODE 6560-50-P

## ENVIRONMENTAL PROTECTION AGENCY

### 40 CFR Part 180

[EPA-HQ-OPP-2013-0411; FRL-9910-52]

### Spirodiclofen; Pesticide Tolerances

**AGENCY:** Environmental Protection Agency (EPA).

**ACTION:** Final rule.

**SUMMARY:** This regulation amends a tolerance for residues of spirodiclofen in or on citrus, oil. Bayer CropScience requested this tolerance amendment under the Federal Food, Drug, and Cosmetic Act (FFDCA).

**DATES:** This regulation is effective [*insert date of publication in the Federal Register*].

Objections and requests for hearings must be received on or before [*insert date 60 days after date of publication in the Federal Register*], and must be filed in accordance with the instructions provided in 40 CFR part 178 (see also Unit I.C. of the

**SUPPLEMENTARY INFORMATION).**

**ADDRESSES:** The docket for this action, identified by docket identification (ID) number EPA-HQ-OPP-2013-0411, is available at <http://www.regulations.gov> or at the Office of Pesticide Programs Regulatory Public Docket (OPP Docket) in the

Environmental Protection Agency Docket Center (EPA/DC), West William Jefferson Clinton Bldg., Rm. 3334, 1301 Constitution Ave., NW., Washington, DC 20460-0001. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room is (202) 566-1744, and the telephone number for the OPP Docket is (703) 305-5805. Please review the visitor instructions and additional information about the docket available at <http://www.epa.gov/dockets>.

**FOR FURTHER INFORMATION CONTACT:** Lois Rossi, Registration Division (7505P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; main telephone number: (703) 305-7090; email address: [RDfRNotices@epa.gov](mailto:RDfRNotices@epa.gov).

## **SUPPLEMENTARY INFORMATION:**

### **I. General Information**

#### *A. Does this Action Apply to Me?*

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. The following list of North American Industrial Classification System (NAICS) codes is not intended to be exhaustive, but rather provides a guide to help readers determine whether this document applies to them. Potentially affected entities may include:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).

- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

*B. How Can I Get Electronic Access to Other Related Information?*

You may access a frequently updated electronic version of EPA's tolerance regulations at 40 CFR part 180 through the Government Printing Office's e-CFR site at [http://www.ecfr.gov/cgi-bin/text-idx?&c=ecfr&tpl=/ecfrbrowse/Title40/40tab\\_02.tpl](http://www.ecfr.gov/cgi-bin/text-idx?&c=ecfr&tpl=/ecfrbrowse/Title40/40tab_02.tpl).

*C. How Can I File an Objection or Hearing Request?*

Under FFDCA section 408(g), 21 U.S.C. 346a, any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. You must file your objection or request a hearing on this regulation in accordance with the instructions provided in 40 CFR part 178. To ensure proper receipt by EPA, you must identify docket ID number EPA-HQ-OPP-2013-0411 in the subject line on the first page of your submission. All objections and requests for a hearing must be in writing, and must be received by the Hearing Clerk on or before *[insert date 60 days after date of publication in the **Federal Register**]*. Addresses for mail and hand delivery of objections and hearing requests are provided in 40 CFR 178.25(b).

In addition to filing an objection or hearing request with the Hearing Clerk as described in 40 CFR part 178, please submit a copy of the filing (excluding any Confidential Business Information (CBI)) for inclusion in the public docket. Information not marked confidential pursuant to 40 CFR part 2 may be disclosed publicly by EPA without prior notice. Submit the non-CBI copy of your objection or hearing request,

identified by docket ID number EPA-HQ-OPP-2013-0411, by one of the following methods:

- *Federal eRulemaking Portal*: <http://www.regulations.gov>. Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be CBI or other information whose disclosure is restricted by statute.

- *Mail*: OPP Docket, Environmental Protection Agency Docket Center (EPA/DC), (28221T), 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001.

- *Hand Delivery*: To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at <http://www.epa.gov/dockets/contacts.html>.

Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at <http://www.epa.gov/dockets>.

## **II. Summary of Petitioned-For Tolerance**

In the **Federal Register** of February 4, 2010 (75 FR 5790) (FRL-8807-5), EPA issued a notice pursuant to section 408(d)(3) of FFDCA, 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide petition (PP 9E7632) by IR-4, 500 College Road East, Suite 201 W., Princeton, NJ 08540. The petition requested that 40 CFR 180.608 be amended by establishing tolerances for residues of the insecticide spiroticlofen, (3-(2,4-dichlorophenyl)-2-oxo-1-oxaspiro[4,5]dec-3-en-4-yl 2,2-dimethylbutanoate), in or on bushberry subgroup 13-07B at 4.0 parts per million (ppm). The petition additionally requested to revise the tolerance expression under paragraphs (a)(1) and (a)(2) to read as

follows: “(a)(1). Tolerances are established for residues of the insecticide spiroticlofen, including its metabolites and degradates. Compliance with the tolerance levels specified is to be determined by measuring only spiroticlofen (3-(2,4-dichlorophenyl)-2-oxo-1-oxaspiro[4,5]dec-3-en-4-yl 2,2-dimethylbutanoate)”; and “(a)(2). Tolerances are established for residues of the insecticide spiroticlofen, including its metabolites and degradates. Compliance with the tolerance levels specified is to be determined by measuring only the sum of spiroticlofen (3-(2,4-dichlorophenyl)-2-oxo-1-oxaspiro[4,5]dec-3-en-4-yl 2,2-dimethylbutanoate) and its metabolite, 3-(2,4-dichlorophenyl)-4-hydroxy-1-oxaspiro[4,5]dec-3-en-2-one, calculated as the stoichiometric equivalent of spiroticlofen.” That notice referenced a summary of the petition prepared on behalf of IR-4 by Bayer CropScience, the registrant, which is available in the docket, <http://www.regulations.gov>.

In the **Federal Register** of March 29, 2011 (76 FR 17374) (FRL-8867-4), EPA issued a notice pursuant to section 408(d)(3) of FFDCA, 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide petition (PP 0E7820) by IR-4, 500 College Rd. East, Suite 201W, Princeton, NJ 08540. The petition requested that 40 CFR 180.608 be amended by establishing tolerances for residues of the insecticide spiroticlofen, (3-(2,4-dichlorophenyl)-2-oxo-1-oxaspiro[4.5]dec-3-en-4-yl 2,2-dimethylbutanoate), in or on sugar apple, cherimoya, atemoya, custard apple, ilama, soursop, biriba, guava, feijoa, jaboticaba, wax jambu, starfruit, passionfruit, persimmon and acerola at 0.45 ppm; and lychee, longan, Spanish lime, rambutan and pulasan at 3.5 ppm. That notice referenced a summary of the petition prepared on behalf of IR-4 by Bayer CropScience, the registrant, which is available in the docket, <http://www.regulations.gov>.

Finally, in the **Federal Register** of July 19, 2013 (78 FR 43115) (FRL-9392-9), EPA issued a document pursuant to FFDCA section 408(d)(3), 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide petition (PP 3F8152) by Bayer CropScience, 2 TW Alexander Dr., Research Triangle Park, NC 27709. The petition requested that 40 CFR 180.608 be amended by amending the established tolerance for residues of the insecticide spiroticlofen, 3-(2,4-dichlorophenyl)-2-oxo-1-oxaspiro[4.5]dec-3-en-4-yl 2,2-dimethylbutanoate, in or on citrus, oil from 20 ppm to 35 ppm. That document referenced a summary of the petition prepared by Bayer CropScience, the registrant, which is available in the docket, <http://www.regulations.gov>. There were no comments received in response to the notice of filing.

IR-4 has since withdrawn PP#s 9E7632 and 0E7820 due to unresolved labeling issues regarding pollinators. However, the EPA has determined that the proposed changes to the tolerance expression under the notice for PP# 9E7632 are appropriate. Additionally, EPA is relying upon the risk assessments supporting those actions in order to amend the citrus, oil tolerance, since the higher citrus, oil level was considered in these assessments. Therefore, risk estimates characterized in the underlying assessments for those actions are considered overestimations of risk, because the uses associated with PP#s 9E7632 and 0E7820 have since been withdrawn; however, those assessments will support the amended citrus, oil tolerance.

### **III. Aggregate Risk Assessment and Determination of Safety**

Section 408(b)(2)(A)(i) of FFDCA allows EPA to establish a tolerance (the legal limit for a pesticide chemical residue in or on a food) only if EPA determines that the

tolerance is “safe.” Section 408(b)(2)(A)(ii) of FFDCA defines “safe” to mean that “there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information.” This includes exposure through drinking water and in residential settings, but does not include occupational exposure. Section 408(b)(2)(C) of FFDCA requires EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing a tolerance and to “ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue....”

Consistent with FFDCA section 408(b)(2)(D), and the factors specified in FFDCA section 408(b)(2)(D), EPA has reviewed the available scientific data and other relevant information in support of this action. EPA has sufficient data to assess the hazards of and to make a determination on aggregate exposure for spirodiclofen including exposure resulting from the tolerances established by this action. EPA's assessment of exposures and risks associated with spirodiclofen follows.

#### *A. Toxicological Profile*

EPA has evaluated the available toxicity data and considered its validity, completeness, and reliability as well as the relationship of the results of the studies to human risk. EPA has also considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children.

Spirodiclofen has a low acute toxicity via the oral, dermal and inhalation routes. It is not an eye or dermal irritant; however, it is a potential skin sensitizer. Following repeated exposures, the primary target organs identified are the adrenal glands in both sexes and testes in males. Increased cytoplasmic vacuolation in the Zona fasciculata of the adrenal cortex was observed in several subchronic and chronic studies in rats, mice and dogs of both sexes. Female rats and dogs appeared to be the more sensitive to adrenal effects, with the dog as the most sensitive species. The effects on the adrenal glands generally coincided with increased adrenal weight. Other organs with histopathology findings reported in male dogs included the testes (vacuolation and hypertrophy/activation of Leydig cells), epididymis (degeneration and/or immaturity of germinal epithelium, oligo- and aspermia), prostate (immaturity signs), and thymus (atrophy). Increased liver weights were also reported in male dogs along with decreases in prostate weights.

The effects reported in chronic dog studies were similar to subchronic studies and occurred at lower administered oral doses of spirodiclofen. As with subchronic studies, histopathology of the adrenal gland revealed an increased incidence of cortical vacuolation in the Zona fasciculata of both sexes. In the testes, increased incidences of Leydig cell vacuolation, slight Leydig cell hypertrophy, and tubular degeneration were observed in males. Other effects reported in chronic studies included decreases in cholesterol and triglycerides, decreased body weights and body-weight gains, increased APh levels and increased vacuolated jejunum enterocytes in rats, and increased incidences of Leydig cell hyperplasia in rats and mice.

There was no evidence of developmental toxicity in the rabbit developmental toxicity study. The rat developmental toxicity study resulted in developmental toxicity (an



increased incidence of slight dilatation of the renal pelvis) at the highest dose tested; a dose which did not cause maternal toxicity. In the 2-generation reproductive toxicity study in rats, developmental effects were observed in F<sub>1</sub> males (delayed sexual maturation, decreased testicular spermatid and epididymal sperm counts/oligospermia; and atrophy of the testes, epididymides, prostate, and seminal vesicles) and F<sub>1</sub> females (increased severity of ovarian luteal cell vacuolation/degeneration), but at a higher dose than the systemic effects seen for parents and offspring.

There was no evidence of neurotoxicity in the acute and subchronic neurotoxicity studies for spirodiclofen. In a developmental neurotoxicity (DNT) study, a decrease in retention was observed in the memory phase of the water maze for postnatal day 60 female offspring at all doses. In this DNT study, the morphometric measurements were not performed at the low- and mid-dose; therefore, another DNT study was conducted using identical experimental conditions as the previous study. The results of the second DNT study demonstrated no treatment-related neurotoxicity, but the two DNT studies for spirodiclofen suggest increased susceptibility of offspring. An acceptable immunotoxicity study, which was reviewed by the EPA after the risk assessment was finalized, showed no treatment related systemic or immunotoxic related effects up to the highest dose tested.

Chronic toxicity and carcinogenicity studies showed an increased incidence of uterine adenocarcinoma in female rats, Leydig cell adenoma in male rats, and liver tumors in mice. The EPA has classified spirodiclofen as “likely to be carcinogenic to humans” by the oral route based on evidence of Leydig cell adenomas in male rat testes, uterine adenomas and/or adenocarcinoma in female rats, and liver tumors in mice. Results of genotoxicity testing were negative.

Specific information on the studies received and the nature of the adverse effects caused by spirodiclofen as well as the no-observed-adverse-effect-level (NOAEL) and the lowest-observed-adverse-effect-level (LOAEL) from the toxicity studies can be found in the document, “Spirodiclofen. Human-Health Risk Assessment for Proposed Uses in/on Sugar Apple, Cherimoya, Atemoya, Custard Apple, Ilama, Soursop, Biriba, Lychee, Longan, Spanish Lime, Rambutan, Pulasan, Guava, Feijoa, Jaboticaba, Wax Jambu, Starfruit, Passionfruit, Persimmon, and Acerola.” At pages 28-30 in docket ID number EPA-HQ-OPP-2013-0411.

*B. Toxicological Points of Departure/Levels of Concern*

Once a pesticide’s toxicological profile is determined, EPA identifies toxicological points of departure (POD) and levels of concern to use in evaluating the risk posed by human exposure to the pesticide. For hazards that have a threshold below which there is no appreciable risk, the toxicological POD is used as the basis for derivation of reference values for risk assessment. PODs are developed based on a careful analysis of the doses in each toxicological study to determine the dose at which no adverse effects are observed (the NOAEL) and the lowest dose at which adverse effects of concern are identified (the LOAEL). Uncertainty/safety factors are used in conjunction with the POD to calculate a safe exposure level - generally referred to as a population-adjusted dose (PAD) or a reference dose (RfD) - and a safe margin of exposure (MOE). For non-threshold risks, the Agency assumes that any amount of exposure will lead to some degree of risk. Thus, the Agency estimates risk in terms of the probability of an occurrence of the adverse effect expected in a lifetime. For more information on the general principles EPA uses in risk characterization and a complete

description of the risk assessment process, see

<http://www.epa.gov/pesticides/factsheets/riskassess.htm>.

A summary of the toxicological endpoints for spirodiclofen used for human risk assessment is shown in Table 1 of this unit.

**Table 1.--Summary of Toxicological Doses and Endpoints for Spirodiclofen for Use in Human Health Risk Assessment**

Exposure/Scenario	Point of Departure and Uncertainty/Safety Factors	RfD, PAD, LOC for Risk Assessment	Study and Toxicological Effects
Acute dietary (All populations, including infants and children)	An appropriate endpoint attributable to a single dose was not identified. Therefore, an acute dietary assessment was not performed.		
Chronic dietary (All populations)	NOAEL= 1.38 mg/kg/day $UF_A = 10x$  $UF_H = 10x$  FQPA SF = 1x	Chronic RfD = 0.014 mg/kg/day  cPAD = 0.014 mg/kg/day	Chronic Oral Toxicity Study in Dogs LOAEL = 4.7 mg/kg/day based on increased relative adrenal weights in both sexes, increased relative testis weights in males and histopathology findings in adrenal glands of both sexes.
Cancer (Oral, dermal, inhalation)	Classification: "Likely to be Carcinogenic to Humans"; $Q_1^* (mg/kg/day)^{-1} = 1.49 \times 10^{-2}$ .		

$UF_A$  = extrapolation from animal to human (interspecies).  $UF_H$  = potential variation in sensitivity among members of the human population (intraspecies). FQPA SF = Food Quality Protection Act Safety Factor. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose. mg/kg/day = milligram/kilogram/day.

### *C. Exposure Assessment*

1. *Dietary exposure from food and feed uses.* In evaluating dietary exposure to spiroticlofen, EPA considered exposure under the petitioned-for tolerances as well as all existing spiroticlofen tolerances in 40 CFR 180.608. EPA assessed dietary exposures from spiroticlofen in food as follows:

i. *Acute exposure.* Quantitative acute dietary exposure and risk assessments are performed for a food-use pesticide, if a toxicological study has indicated the possibility of an effect of concern occurring as a result of a 1-day or single exposure. No such effects were identified in the toxicological studies for spiroticlofen; therefore, a quantitative acute dietary exposure assessment is unnecessary.

ii. *Chronic exposure.* In conducting the chronic dietary exposure assessment EPA used the food consumption data from the United States Department of Agriculture (USDA) 1994-1996 and 1998 Nationwide Continuing Surveys of Food Intake by Individuals (CSFII). As to residue levels in food, EPA utilized average field trial residues; experimentally determined processing factors for citrus fruit, pome fruit and grape; and Dietary Exposure Evaluation Model (DEEM (ver 7.81)) default processing factors for the remaining processed commodities. The assessment also utilized percent crop treated for new uses (PCTn) on hops and blueberry, and percent crop treated (PCT) estimates for several other registered commodities.

iii. *Cancer.* EPA determines whether quantitative cancer exposure and risk assessments are appropriate for a food-use pesticide based on the weight of the evidence

from cancer studies and other relevant data. If quantitative cancer risk assessment is appropriate, Cancer risk may be quantified using a linear or nonlinear approach. If sufficient information on the carcinogenic mode of action is available, a threshold or nonlinear approach is used and a cancer RfD is calculated based on an earlier noncancer key event. If carcinogenic mode of action data are not available, or if the mode of action data determines a mutagenic mode of action, a default linear cancer slope factor approach is utilized. Based on the data summarized in Unit III.A., EPA has concluded that spirodiclofen should be classified as “Likely to be Carcinogenic to Humans” and a linear approach has been used to quantify cancer risk. Cancer risk was quantified using the same food residue estimates as discussed in Unit III.C.1.ii.

iv. *Anticipated residue and percent crop treated (PCT) information.* Section 408(b)(2)(E) of FFDCA authorizes EPA to use available data and information on the anticipated residue levels of pesticide residues in food and the actual levels of pesticide residues that have been measured in food. If EPA relies on such information, EPA must require pursuant to FFDCA section 408(f)(1) that data be provided 5 years after the tolerance is established, modified, or left in effect, demonstrating that the levels in food are not above the levels anticipated. For the present action, EPA will issue such data calls as are required by FFDCA section 408(b)(2)(E) and authorized under FFDCA section 408(f)(1). Data will be required to be submitted no later than 5 years from the date of issuance of these tolerances.

Section 408(b)(2)(F) of FFDCA states that the Agency may use data on the actual percent of food treated for assessing chronic dietary risk only if:

- Condition a: The data used are reliable and provide a valid basis to show what percentage of the food derived from such crop is likely to contain the pesticide residue.
- Condition b: The exposure estimate does not underestimate exposure for any significant subpopulation group.
- Condition c: Data are available on pesticide use and food consumption in a particular area, the exposure estimate does not understate exposure for the population in such area.

In addition, the Agency must provide for periodic evaluation of any estimates used. To provide for the periodic evaluation of the estimate of PCT as required by FFDCA section 408(b)(2)(F), EPA may require registrants to submit data on PCT.

The Agency estimated the PCT for existing uses as follows: Almond, 5%; apple, 5%; apricot, 5%; cherry, 2%; grapefruit, 50%; grape, raisin, 10%; grape, table, 30%; grape, wine, 5%; hazelnuts, 2%; lemon, 1%; nectarine, 10%; orange, 10%; peach, 5%; pear, 10%; pecan, 2%; pistachio, 1%; plum/prune, 5%; and walnut, 5%.

In most cases, EPA uses available data from USDA/National Agricultural Statistics Service (USDA/NASS), proprietary market surveys, and the National Pesticide Use Database for the chemical/crop combination for the most recent 6-7 years. EPA uses an average PCT for chronic dietary risk analysis. The average PCT figure for each existing use is derived by combining available public and private market survey data for that use, averaging across all observations, and rounding to the nearest 5%, except for those situations in which the average PCT is less than one. In those cases, 1% is used as the average PCT and 2.5% is used as the maximum PCT. EPA uses a maximum PCT for

acute dietary risk analysis. The maximum PCT figure is the highest observed maximum value reported within the recent 6 years of available public and private market survey data for the existing use and rounded up to the nearest multiple of 5%.

The Agency estimated the PCT for new uses as follows: Blueberry, 2%; and hops, 92%.

In the **Federal Register** of May 7, 2008 (73 FR 25533) (FRL-8362-2), the Agency estimated the PCT for the proposed use of spiroticlofen on hops to be 92%. Since spiroticlofen has only been registered on hops since 2008, EPA relied on the previously estimated PCT for hops.

The EPA estimate of the percent PCT for these new uses of spiroticlofen represents the upper bound of use expected during the pesticide's initial five years of registration; that is, the PCT for spiroticlofen is a threshold of use that EPA is reasonably certain will not be exceeded for this registered use site. The PCT recommended for use in the chronic dietary assessment is calculated as the average PCT of the miticide with the highest usage (i.e., the miticides with the greatest PCT) on that crop over the three most recent years of available data. The PCT recommended for use in the chronic dietary assessment is 2% for blueberries and 92% for hops. Comparisons are only made among pesticides of the same pesticide type (i.e., the miticide with the highest usage on the use crop is selected for comparison with a new miticide). The highest miticide PCT included in the estimation may not be the same for each year since different miticides may have the highest usage in different years.

Typically, EPA uses USDA/NASS surveys as the source data because they are publicly available and directly report values for PCT. When a specific use crop is not reported by USDA/NASS, EPA uses proprietary data and calculates the PCT based on reported data on acres treated and acres grown. If no proprietary data are available, EPA may extrapolate PCT for new uses from other crops if the production area and pest spectrum are substantially similar.

A retrospective analysis to validate this approach shows few cases where the PCT for the highest miticides were exceeded (EPA, 2006). Further review of these cases identified factors contributing to the exceptionally high use of a new pesticide. To evaluate whether the PCT for spiroticlofen could be exceeded, EPA considered whether or not there may be unusually high pest pressure, as indicated in emergency exemption requests for spiroticlofen, the pest spectrum of the new pesticide in comparison with the highest miticides, whether or not the highest miticides are well-established for that use and whether or not pest resistance issues with past miticides provide spiroticlofen with significant market potential. Given currently available information, the Agency concludes that it is unlikely that actual PCT for spiroticlofen will exceed the estimated PCT for new uses during the next five years.

The Agency believes that the three conditions discussed in Unit III.C.1.iv. have been met. With respect to Condition a, PCT estimates are derived from Federal and private market survey data, which are reliable and have a valid basis. The Agency is reasonably certain that the percentage of the food treated is not likely to be an underestimation. As to Conditions b and c, regional consumption information and consumption information for significant subpopulations is taken into account through



EPA's computer-based model for evaluating the exposure of significant subpopulations including several regional groups. Use of this consumption information in EPA's risk assessment process ensures that EPA's exposure estimate does not understate exposure for any significant subpopulation group and allows the Agency to be reasonably certain that no regional population is exposed to residue levels higher than those estimated by the Agency. Other than the data available through national food consumption surveys, EPA does not have available reliable information on the regional consumption of food to which spirodiclofen may be applied in a particular area.

2. *Dietary exposure from drinking water.* EPA concluded that the residues of concern in drinking water for purposes of risk assessment are spirodiclofen and its three metabolites (BAJ 2510, BAJ 2740-dihydroxy, and BAJ 2740-ketohydroxy). Therefore, the Agency used screening level water exposure models in the dietary exposure analysis and risk assessment for spirodiclofen and its metabolites in drinking water. These simulation models take into account data on the physical, chemical, and fate/transport characteristics of spirodiclofen and its metabolites. Further information regarding EPA drinking water models used in pesticide exposure assessment can be found at <http://www.epa.gov/oppefed1/models/water/index.htm>.

Based on the Pesticide Root Zone Model /Exposure Analysis Modeling System (PRZM/EXAMS) and Screening Concentration in Ground Water (SCI-GROW) models, the estimated drinking water concentrations (EDWCs) of spirodiclofen and its metabolites for chronic exposures for non-cancer assessments are estimated to be 4.99 parts per billion (ppb) for surface water and 0.44 ppb for ground water. The EDWCs for

chronic exposures for cancer assessments are estimated to be 1.67 ppb for surface water and 0.44 ppb for ground water.

Modeled estimates of drinking water concentrations were directly entered into the dietary exposure model. For chronic dietary risk assessment, the water concentration of value 4.99 ppb was used to assess the contribution to drinking water. For cancer dietary risk assessment, the water concentration of value 1.67 ppb was used to assess the contribution to drinking water.

3. *From non-dietary exposure.* The term “residential exposure” is used in this document to refer to non-occupational, non-dietary exposure (e.g., for lawn and garden pest control, indoor pest control, termiticides, and flea and tick control on pets). Spirodiclofen is not registered for any specific use patterns that would result in residential exposure.

4. *Cumulative effects from substances with a common mechanism of toxicity.* Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider “available information” concerning the cumulative effects of a particular pesticide's residues and “other substances that have a common mechanism of toxicity.” EPA has not found spirodiclofen to share a common mechanism of toxicity with any other substances, and spirodiclofen does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has assumed that spirodiclofen does not have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism of toxicity and to evaluate the

cumulative effects of such chemicals, see EPA's website at

<http://www.epa.gov/pesticides/cumulative>.

*D. Safety Factor for Infants and Children*

1. *In general.* Section 408(b)(2)(C) of FFDCA provides that EPA shall apply an additional tenfold (10X) margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the database on toxicity and exposure unless EPA determines based on reliable data that a different margin of safety will be safe for infants and children. This additional margin of safety is commonly referred to as the FQPA SF. In applying this provision, EPA either retains the default value of 10X, or uses a different additional safety factor when reliable data available to EPA support the choice of a different factor.

2. *Prenatal and postnatal sensitivity.* The spirodiclofen toxicity database is adequate to evaluate the potential increased susceptibility of infants and children, and includes developmental toxicity studies in rat and rabbit, a 2-generation toxicity study in rat, and two rat DNT studies. There is no evidence of increased susceptibility in the rabbit developmental toxicity study or in the 2-generation rat reproductive toxicity study following *in utero*/pre- and postnatal exposures of spirodiclofen. However, evidence for quantitative susceptibility was observed in a rat developmental toxicity study, where an increased incidence of slight dilatation of the renal pelvis was observed at the highest dose tested (1,000 mg/kg/day) in the absence of maternal toxicity. Additionally, two rat DNT studies are available. The first study demonstrated increased quantitative susceptibility of offspring based on the observed decreased retention in the memory

phase of the water maze for postnatal day 60 female offspring at all doses and changes in brain morphometric parameters at the highest dose tested of 135.9 mg/kg/day (including caudate putamen, parietal cortex, hippocampal gyrus, and dentate gyrus); there was no maternal toxicity noted at any dose. EPA requested information concerning the brain morphometric parameters in the low- and mid doses with the petitioner indicating that the brain tissues were not appropriately preserved and analysis was therefore not possible. As a result, a second rat DNT study was submitted which also indicated increased susceptibility in offspring based on decreased pre-weaning body weight and body weight gain in males and females and decreased post-weaning body weights in males. The second rat DNT demonstrated no treatment-related neurotoxicity in the offspring.

3. *Conclusion.* EPA has determined that reliable data show the safety of infants and children would be adequately protected if the FQPA SF were reduced to 1X. That decision is based on the following findings:

i. The toxicity database for spiroadiclofen is complete. Changes to 40 CFR Part 158 require immunotoxicity testing (OPPTS Guideline 870.7800) for pesticide registration. At the time of the last completed risk assessment for spiroadiclofen, which was finalized on November 11, 2011, an immunotoxicity study was a data gap in the toxicity database. However, since the time of the risk assessment, EPA has received and reviewed an acceptable immunotoxicity study for spiroadiclofen. Upon review of the study, the Agency has determined that there is no treatment related systemic or immunotoxic related effects. Therefore, the immunotoxicity study does not impact the findings of the 2011 risk assessment. Additionally, EPA has determined a subchronic inhalation toxicity study is not required for spiroadiclofen at this time. This approach

considered all of the available hazard and exposure information for spirodiclofen, including: (1) Its low acute inhalation toxicity; (2) the lowest short- and intermediate-term MOEs calculated using an oral POD are 6,200 and 1,000 respectively; and (3) its physical and chemical properties, including its low volatility. Therefore, an additional UF is not needed to account for the lack of this study.

ii. Two DNT studies have been submitted and reviewed by the EPA. The Agency has determined that there is no concern for the increased quantitative susceptibility seen in the first DNT study because the results were not reproduced in the second DNT study conducted using identical doses and experimental conditions. The second DNT provided no evidence of neurotoxicity, and concern for the increased quantitative susceptibility (slight changes in body weights) noted in this study is low because there is a well-established NOAEL, only marginal developmental toxicity was noted, and all developmental/functional parameters were comparable to controls. In addition, doses selected for risk assessment of spirodiclofen are much lower than the dose where the effects in the second DNT were noted. Finally, there was no evidence of neurotoxicity or neuropathology in the acute and subchronic neurotoxicity studies. Therefore, there is no need for an additional UF to account for neurotoxicity. Additional information about the two DNT studies can be found at <http://www.regulations.gov> in the **Federal Register** of May 7, 2008 (<http://www.epa.gov/fedrgstr/EPA-PEST/2008/May/Day-07/p9826.htm>).

iii. Quantitative susceptibility was noted in the developmental toxicity study in rats. However, EPA determined that the degree of concern is low for the noted effects because the increased incidence of slight renal pelvic dilation was observed only at the highest dose tested, in the absence of statistical significance and dose response.

Additionally, renal pelvic dilation was considered to be a developmental delay and not a severe effect for developmental toxicity. The low background incidences in this study may also be idiosyncratic to this strain (Wistar) of rats since renal pelvic dilations are commonly seen at higher incidences in other strains (Sprague-Dawley or Fisher) of rats. Furthermore, there is a well-established NOAEL at which all developmental/functional parameters were comparable to controls, and lower doses are being used for the risk assessment of spirodiclofen. As noted above, concern is low for the increased quantitative susceptibility noted in offspring in the DNT studies. There was no evidence of increased susceptibility in the developmental toxicity study in rabbits or the 2-generation reproduction study in rats. Therefore, there are no residual concerns regarding developmental effects in the young.

iv. There are no residual uncertainties identified in the exposure databases. The chronic and cancer dietary exposure assessments were refined, utilizing average field trial residues; experimentally determined processing factors for citrus fruit, pome fruit, and grape; and DEEM (ver. 7.81) default processing factors for the remaining processed commodities. The assessment also included PCTn estimates for hops and blueberry and PCT data for several additional registered commodities. EPA made conservative (protective) assumptions in the ground water and surface water modeling used to assess exposure to spirodiclofen and its metabolites in drinking water. These assessments will not underestimate the exposure and risks posed by spirodiclofen.

#### *E. Aggregate Risks and Determination of Safety*

EPA determines whether acute and chronic dietary pesticide exposures are safe by comparing aggregate exposure estimates to the acute PAD (aPAD) and chronic PAD (cPAD). For linear cancer risks, EPA calculates the lifetime probability of acquiring cancer given the estimated aggregate exposure. Short-, intermediate-, and chronic-term risks are evaluated by comparing the estimated aggregate food, water, and residential exposure to the appropriate PODs to ensure that an adequate MOE exists.

1. *Acute risk.* An acute aggregate risk assessment takes into account acute exposure estimates from dietary consumption of food and drinking water. No adverse effect resulting from a single oral exposure was identified and no acute dietary endpoint was selected. Therefore, spirodiclofen is not expected to pose an acute risk.

2. *Chronic risk.* Using the exposure assumptions described in this unit for chronic exposure, EPA has concluded that chronic exposure to spirodiclofen from food and water will utilize 3.2 % of the cPAD for children 1-2 years old, the population group receiving the greatest exposure. There are no residential uses for spirodiclofen.

3. *Short- and intermediate-term risk.* Short- and intermediate-term aggregate exposure takes into account short- and intermediate-term residential exposure plus chronic exposure to food and water (considered to be a background exposure level). A short- and intermediate-term adverse effect was identified; however, spirodiclofen is not registered for any use patterns that would result in short- or intermediate-term residential exposure. Short- and intermediate-term risk is assessed based on short- and intermediate-term residential exposure plus chronic dietary exposure. Because there are no short- or intermediate-term residential exposures and chronic dietary exposure has already been

assessed under the appropriately protective cPAD (which is at least as protective as the POD used to assess short- and intermediate-term risk), no further assessment of short- or intermediate-term risk is necessary, and EPA relies on the chronic dietary risk assessment for evaluating short- and intermediate-term risk for spirodiclofen.

4. *Aggregate cancer risk for U.S. population.* Using the exposure assumptions described in Unit III.C.1.iii., EPA has concluded the cancer risk from food and water for all existing and proposed spirodiclofen uses will result in a lifetime cancer risk of  $3 \times 10^{-6}$ . EPA generally considers cancer risks in the range of  $10^{-6}$  or less to be negligible. The precision which can be assumed for cancer risk estimates is best described by rounding to the nearest integral order of magnitude on the log scale; for example, risks falling between  $3 \times 10^{-7}$  and  $3 \times 10^{-6}$  are expressed as risks in the range of  $10^{-6}$ . Considering the precision with which cancer hazard can be estimated, the conservativeness of low-dose linear extrapolation, and the rounding procedure described above in this unit, cancer risk should generally not be assumed to exceed the benchmark level of concern of the range of  $10^{-6}$  until the calculated risk exceeds approximately  $3 \times 10^{-6}$ . This is particularly the case where some conservatism is maintained in the exposure assessment.

For the following reasons, EPA concludes that there are conservatisms in the spirodiclofen exposure assessment. Based on a critical commodity analysis conducted in DEEM-Food Commodity Intake Database (DEEM-FCID)<sup>TM</sup>, the major contributors to the cancer risk were hops (44% of the total exposure) and water (21% of the total exposure). EPA notes the following conservative assumptions, which were incorporated into the cancer analysis for hops and water:



i. *Hops*. DEEM-FCID™ assumes that 100% of the residues in hops are transferred to beer during the brewing process (no residues remain in/on the spent hops). Since spirodiclofen has low water solubility, this is a conservative assumption. Additionally, the assessment assumed a PCT estimate of 92% for hops; PCT estimates for new uses are designed to provide a conservative estimate of the actual PCT estimates; and

ii. *Drinking water*. The water residue estimate assumed 87% of the basin is cropped with 100% of the crops treated at the maximum labeled rate.

Therefore, EPA concludes that the cancer risk estimate provided in this assessment is conservative and actual cancer risk will be lower than the estimate provided in this document.

5. *Determination of safety*. Based on these risk assessments, EPA concludes that there is a reasonable certainty that no harm will result to the general population, or to infants and children from aggregate exposure to spirodiclofen residues.

#### **IV. Other Considerations**

##### *A. Analytical Enforcement Methodology*

Adequate enforcement methodology, a liquid chromatography/mass spectrometry/mass spectrometry (LC/MS/MS) method, is available to enforce the tolerance expression.

The method may be requested from: Chief, Analytical Chemistry Branch, Environmental Science Center, 701 Mapes Rd., Ft. Meade, MD 20755-5350; telephone number: (410) 305-2905; email address: [residuemethods@epa.gov](mailto:residuemethods@epa.gov).

### *B. International Residue Limits*

In making its tolerance decisions, EPA seeks to harmonize U.S. tolerances with international standards whenever possible, consistent with U.S. food safety standards and agricultural practices. EPA considers the international maximum residue limits (MRLs) established by the Codex Alimentarius Commission (Codex), as required by FFDCA section 408(b)(4). The Codex Alimentarius is a joint United Nations Food and Agriculture Organization/World Health Organization food standards program, and it is recognized as an international food safety standards-setting organization in trade agreements to which the United States is a party. EPA may establish a tolerance that is different from a Codex MRL; however, FFDCA section 408(b)(4) requires that EPA explain the reasons for departing from the Codex level.

The Codex has not established a MRL for spiroticlofen in or on citrus oil.

## **V. Conclusion**

Therefore, a tolerance for residues of spiroticlofen, 3-(2,4-dichlorophenyl)-2-oxo-1-oxaspiro[4.5]dec-3-en-4-yl 2,2-dimethylbutanoate, in or on citrus, oil is amended from 20 ppm to 35 ppm. Additionally, the tolerance expression is amended for spiroticlofen in order to clarify (1) that, as provided in FFDCA section 408(a)(3), the tolerance covers metabolites and degradates of spiroticlofen not specifically mentioned; and (2) that compliance with the specified tolerance levels is to be determined by measuring only spiroticlofen.

## **VI. Statutory and Executive Order Reviews**

This final rule establishes tolerances under FFDCA section 408(d) in response to a petition submitted to the Agency. The Office of Management and Budget (OMB) has exempted these types of actions from review under Executive Order 12866, entitled “Regulatory Planning and Review” (58 FR 51735, October 4, 1993). Because this final rule has been exempted from review under Executive Order 12866, this final rule is not subject to Executive Order 13211, entitled “Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use” (66 FR 28355, May 22, 2001) or Executive Order 13045, entitled “Protection of Children from Environmental Health Risks and Safety Risks” (62 FR 19885, April 23, 1997). This final rule does not contain any information collections subject to OMB approval under the Paperwork Reduction Act (PRA) (44 U.S.C. 3501 *et seq.*), nor does it require any special considerations under Executive Order 12898, entitled “Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations” (59 FR 7629, February 16, 1994).

Since tolerances and exemptions that are established on the basis of a petition under FFDCA section 408(d), such as the tolerance in this final rule, do not require the issuance of a proposed rule, the requirements of the Regulatory Flexibility Act (RFA) (5 U.S.C. 601 *et seq.*), do not apply.

This final rule directly regulates growers, food processors, food handlers, and food retailers, not States or tribes, nor does this action alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of FFDCA section 408(n)(4). As such, the Agency has determined that this action will not have a substantial direct effect on States or tribal governments, on the relationship between the national government and the States or tribal governments, or on

the distribution of power and responsibilities among the various levels of government or between the Federal Government and Indian tribes. Thus, the Agency has determined that Executive Order 13132, entitled “Federalism” (64 FR 43255, August 10, 1999) and Executive Order 13175, entitled “Consultation and Coordination with Indian Tribal Governments” (65 FR 67249, November 9, 2000) do not apply to this final rule. In addition, this final rule does not impose any enforceable duty or contain any unfunded mandate as described under Title II of the Unfunded Mandates Reform Act of 1995 (UMRA) (2 U.S.C. 1501 *et seq.*).

This action does not involve any technical standards that would require Agency consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act of 1995 (NTTAA) (15 U.S.C. 272 note).

## **VII. Congressional Review Act**

Pursuant to the Congressional Review Act (5 U.S.C. 801 *et seq.*), EPA will submit a report containing this rule and other required information to the U.S. Senate, the U.S. House of Representatives, and the Comptroller General of the United States prior to publication of the rule in the **Federal Register**. This action is not a “major rule” as defined by 5 U.S.C. 804(2).

**List of Subjects in 40 CFR Part 180**

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: June 2, 2014.

Lois Rossi,

*Director, Registration Division, Office of Pesticide Programs.*

Therefore, 40 CFR chapter I is amended as follows:

**PART 180--[AMENDED]**

1. The authority citation for part 180 continues to read as follows:

**Authority:** 21 U.S.C. 321(q), 346a and 371.

2. Section 180.608 is amended by:

- a. Revising the introductory text of paragraphs (a)(1) and (a)(2); and
- b. Revising the commodity “Citrus, oil” in the table in paragraph (a)(1) to read as follows:

**§ 180.608 Spirodiclofen; tolerances for residues.**

(a) *General.* (1) Tolerances are established for residues of spirodiclofen, including its metabolites and degradates, in or on the commodities listed below.

Compliance with the following tolerance levels is to be determined by measuring only spirodiclofen (3-(2,4-dichlorophenyl)-2-oxo-1-oxaspiro[4.5]dec-3-en-4-yl 2,2-dimethylbutanoate).

Commodity	Parts per million
* * *	* * * *
Citrus, oil	35
* * *	* * * *

(2) Tolerances are established for residues of spirodiclofen, including its metabolites and degradates, in or on the commodities listed below. Compliance with the following tolerance levels is to be determined by measuring only spirodiclofen (3-(2,4-dichlorophenyl)-2-oxo-1-oxaspiro[4.5]dec-3-en-4-yl 2,2-dimethylbutanoate) and its metabolite 3-(2,4-dichlorophenyl)-4-hydroxy-1-oxaspiro[4,5] dec-3-en-2-one, calculated as the stoichiometric equivalent of spirodiclofen.

\* \* \* \*

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